CHAPTER SIX

Interaction between Noise and Chemicals Found in the Workplace

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As discussed in earlier chapters, several factors have been studied to try to understand why the prevalence and degree of noise-induced hearing loss can vary so much within a group and among groups. Some of the factors studied include variations in exposure, age, gender, race, and general health indicators, such as blood pressure and use of certain medications. The focus of the present chapter will be on the ototoxicity (the toxic effects on hearing), industrial chemicals and, their interaction with noise.

Hearing loss apart from noise can occur after ingestion of certain drugs due to their effects on the auditory system or brain. The ototoxicity of therapeutic drugs has been recognized since the 19th Century. The first reports associated the intake of certain drugs such as quinine and acetyl salicylic acid (ASA) with temporary hearing loss as well as dizziness and tinnitus. In the 1940s, permanent damage to the cochlea (sensory end organ for hearing) was reported in several patients treated with the newly discovered drug for treatment of tuberculosis, the aminoglycoside antibiotic streptomycin. Today there are many well-known ototoxic drugs used in clinical sit-

uations. Most of them (antibiotics, chemotherapeutics, diuretics and anti-malaria drugs) are used despite these negative side effects in order to treat other serious, sometimes life-threatening conditions.

By comparison, only recently the ototoxicity of chemicals found in the environment from contaminants in air, food or water, and in the workplace, became a concern for audiologists and other healthcare professionals. Initially, there were just isolated reports following acute intoxications, poisonings, and observations that hearing losses were more common and sometimes more severe in work settings where chemical exposures occurred. Other studies on the neurotoxicity of chemicals indicated that chemicals were also damaging more central portions of the auditory system. Following these reports, other research laboratories started investigating the ototoxic properties of chemical agents and identified ototoxic properties in a few classes of industrial chemicals: metals, solvents, asphyxiants, pesticides, and polychlorinated biphenyls (PCBs).

Studies conducted with experimental animals have shown that some toxicants can reach the inner ear through the blood stream. They were found in inner ear fluids (endolymph and perilymph, discussed in more detail in Chapter 2) and have caused damage to some of the inner ear structures and have impaired functions. Some of these chemicals are also damaging to the nerves. The onset, site, mechanism and extent of ototoxic damage of these toxicants vary according to risk factors that include: type of chemical, interactions, exposure level and duration of administration, as is the case with ototoxic therapeutic drugs such as cisplatin (used in chemotherapy) and aminoglycoside antibiotics.

The hearing loss caused by chemicals can be very similar to a hearing loss caused by excessive noise. Since noise exposure is so common in modern societies, this might explain the delay in recognizing the risk to hearing that these chemicals can pose. Also, in most cases, the hearing loss as detected by a pure tone audiometric test is often just mild to moderate. Moreover, the results of the audiometric test for a noise-induced hearing loss and an ototoxic hearing loss can have the same configuration on the audiogram. It is also known that generally, in these disorders, hearing loss is bilateral, with symmetrical patterns on the audiogram for both ears, and is often irreversible. Hearing loss starts in the high frequencies (higher pitches, 3000-6000 Hz), and progresses at a rate determined by exposure to various risk factors. Hearing loss caused by ototoxicity is usually cochlear (that is, sensorineural).

Pure tone audiometry is a basic clinical test that is used to determine a person's hearing sensitivity at specific frequencies, i.e., the softest sound that can be perceived in a quiet environment. It clearly identifies various characteristics of the problem, but not its cause. Other hearing tests such as word recognition or otoacoustic emission tests (described in Chapters 1 and 2) examine other auditory functions. These tests can in some cases help differentiate the effects of chemicals from the effects of noise, since chemicals might affect more central portions of the auditory system (nerves or nuclei of the central nervous system, the pathways to the brain or in the brain itself). This suggests that the impact of hearing loss on the worker's life may be more pronounced, because not only will sounds be perceived as less loud, but also as distorted. Word recognition may be compromised, particularly in background noise, making it difficult, for instance, to hold a conversation in a busy restaurant or at a party.

Often, it can be challenging to identify the precise cause of a hearing loss. Information on word recognition difficulties or other auditory tests that are inconsistent with pure tone audiometric results can indicate the need for further hearing testing to complement the assessment.

As mentioned earlier, noise exposure can interact with several toxicants. In some cases, a substance will not cause hearing loss by itself, but can exacerbate a hearing loss caused by noise. This process is called *potentiation*. Also, a substance that is ototoxic can interact synergistically with noise, (i.e., the combined biological effect of two hazards is greater than either alone).

Table 6-1 summarizes key descriptors of the effects of the ototoxicants investigated to date. Table 6-2 lists the studied ototoxicants, by class, by the type of possible interaction with noise and sources of exposure. It's important to remember that exposures to these chemicals can occur outside the work environment. Non-occupational exposure can happen from any activities that involve solvents, paint, polyur-ethanes, paint thinners, degreasers, and fuels.

It's very difficult to predict the exact conditions (such as the exact concentration or period of time) one would need to be exposed to the studied chemicals to suffer an effect. The dose-response lowest observed adverse effect level (LOAEL) and no-observed adverse effect level (NOAEL) have been identified in animal experiments for a few substances. In some cases, chemical exposures increase the adverse effects of noise. Exposures to several stressors, such as hysical demands, or smoking can also modify the LOAEL and

Descriptors of Ototoxic Effects of Chemicals from Animal Experiments

- Effects observed in different species: rats, mice, guinea pigs, monkeys
- Mainly cochlear lesion
- Medium frequency audiometric range
- Noise exposure not a necessary condition for evaluated solvents, metals or insecticides but necessary for carbon monoxide, hydrogen cyanide or acrylonitrile
- Noise interaction/synergism
- Additive effect between solvents

Descriptors of Ototoxic Effects of Chemicals from Clincal and Field Studies

- Environmental (contaminated water, food or from dust, etc) and occupational exposures to chemicals can affect auditory system
- Auditory effects have been reported following intentional in halation or accidental poisoning
- Increased prevalence of hearing loss as registered in pure tone audiograms (mild to moderate, bilateral, high frequency audiometric loss)
- Interaction with noise not clearly identified as synergist or additive, due to limitations in exposure history ascertainment
- Cochlear and retrocochlear or central lesion sites
- Poorer than expected performance on tests that evaluate more central portions of auditory system

Table 6-1: General descriptors of ototoxic effects of chemicals found in the environment from animal experiments, clinical and field studies

NOAEL of the chemical agent. For example, a single exposure to a particular chemical in quiet may not elicit a toxic response, yet, the same exposure in the presence of high-level noise can create a hearing loss (when either alone would not). Moreover, there's a difference in the lowest level necessary to cause an effect in humans and experimental animals. When compared, the levels necessary for an effect seems lower (posing a greater risk) in humans than in animals.

Table 6-2: Substances with ototoxic properties, their interaction with noise and possible sources of exposure

Substance	Interaction with noise	Industrial uses http://hazmap.nlm.nih.gov/
SOLVENTS		
Styrene	Synergism	Manufacture of synthetic rubber, fibreglass reinforced polyester products. Part of floor waxes, polishes, paints, adhesives, metal cleaners and vanishes.
Toluene	Synergism	Solvent carrier in paints, thinners, adhesives, inks, glues,enamels,and component of gasoline. Production, handling and use of toluene and toluene containing products, e.g. chemical laboratory workers, gasoline blenders, lacquer workers, paint and paint thinner makers, petrochemical workers, maintenance workers, painters and printers. One of the 50 most commonly produced industrial chemicals.
Xylenes	No data	Present in motor and aviation fuel, but is also used as solvent in the paint, printing, rubber and leather industries.
Trichloro-ethylene(TCE)	Synergism	Degreaser in metal cleaning operations; in textile cleaning. Also used as a paint stripper, adhesive solvent, ingredient in paints /varnishes, and in manufacture of organic chemicals.
Ethylbenzene	Additive/ Synergism	Unusual in the work environment. As part of mixed xylenes, ethylbenzene is one of many solvents in solvent mixtures (paints, lacquers, rubber/chemical manufacturing industries).
Chlorobenzene	No data	Raw material in chemical synthesis, as a solvent and detergent.
n-Hexane	No data	Production of tires, in glues for the manufacture of leather products and textiles, as a raw material in the production of other chemicals, and as an additive to gasoline.
n-Heptane	No data	Anesthetic, solvent, organic synthesis, preparation of laboratory reagents.
Carbon disulphide	No data	Manufacture of regenerated cellulose rayon (by the viscose process) and cellophane, carbon tetrachloride, the vulcanisation and manufacture of rubber and rubber ac cessories, the production of resins, xanthates, thiocyanates, plywood adhesives, flotation agents, solvent and spinning-solution applications, conversion and processing of hydrocarbons, petroleum-well cleaning, brightening of precious metals in electroplating, rust removal from metals, removal and recovery of metals and other elements from waste water and other media, in refining petroleum jelly and paraffin, and in extracting oil from bones, olives, and rags.

Substance	Interaction with noise	Industrial uses http://hazmap.nlm.nih.gov/
METALS		
Lead	No data	Manufacture of car batteries, sheet metal, pipes, and foil, in mining and in polluted environments. Individuals employed in any of these occupations may bring lead dust on their bodies or clothing into their homes.
Mercury	No data	Present in contaminated air, water, and food, or through the skin. Workers may be exposed to mercury and its compounds in mercury mines and refineries, chemical manufacturing, fluorescent light bulb manufacturing, dental/health fields, fossil fuel power plants, and metal smeltering.
Organotins or Trimethyltins	No data	Production of plastics in the chemical industry and as biocides in antifouling boat bottom paints.
ASPHYXIANTS		
Carbon Monoxide	Potentiation	Common contaminant. Product of incomplete combustion of fuels, coal, oil, and wood, also present in gasoline-powered engine exhaust and tobacco smoke. Forging, melting, pouring and welding metals, in farm operations, fire fighting, sewage and water treatment jobs.
Hydrogen Cyanide	Potentiation	Production of acrylic resin plastic, and other organic chemical products, tempering steel, dyeing, explosives, and engraving. Present in vehicle exhaust, in tobacco smoke, and in the smoke of burning nitrogen-containing plastics.
Acrylonitrile	Potentiation	Production of other chemicals such as plastics, synthetic rubber, and acrylic fibres, and is one of the 50 most commonly produced industrial chemicals.
3,3'-Iminodi-propionitrile	No data	No reports on occupational exposures to and no OELs for IDPN were located.
Pesticides	No data	Herbicides, insecticides, fungicides, and fumigants.
Polychlorinated biphenyls (PCBs)	No data	Repair and maintenance of PCB transformers, accidents, fires, or spills involving PCB transformers and older computers and instruments, and disposal of PCB materials. Caulking materials, elastic sealants, and heat insulation have also been known to contain PCBs.

Researchers in France and Denmark have demonstrated in studies with experimental animals that by adding other stressors such as impact noise, carbon monoxide or ensuring that the animals are active during chemical exposure, the lowest level of solvent exposure was reduced before it elicited an auditory effect. This may be true because humans are generally exposed to solvents in combination with a multitude of other factors (several exposures, physical demands, and so forth.) whereas animal experiments typically involve isolated solvent exposures. Another complication in determining the concentration needed for a hearing loss to occur in humans exists because often individuals are not aware of the concentration they've been exposed to, and because many factors can interact in causing an effect. However, unfortunately cases of hearing loss have been observed after exposures that were within permissible limits.

Another challenge in this area is that the number of chemicals studied to date is very small, particularly when one considers the enormous number of existing industrial chemicals and the thousands of new ones placed on the market every year. It's therefore of crucial importance to understand the mechanisms by which chemicals affect the auditory system.

Several different mechanisms can take place and result in an auditory disorder. Some common features can be found between damaging mechanisms resulting from the physical agent (noise) and some of the ototoxic chemicals. A hypothesis is that the damage to the hair cells is caused by the formation of free radicals, so-called reactive oxygen species (ROS). Free radical and reactive oxygen species are ions (very small molecules) that are highly reactive. ROS form as a natural by-product of the normal metabolism of oxygen. During stressful situations ROS levels can increase dramatically, which can result in damage to cell structures. One can be exposed to free radicals through by-products of normal processes that take place in your body, when the body breaks down certain medicines, and through pollutants. The generation of free radicals has been associated with cellular injury in different organ systems. It's considered a basic mechanism of toxicity, and is thought to be part of the mechanism underlying noise-induced hearing loss (explained in further detail in Chapter 2). Other chemicals such as metals and pesticides may affect both the cochlea and the central auditory pathways, depending on the substance.

When specific ototoxicity information is not available on a partic-

ular chemical, individuals concerned about the potential risk factors should look for information on the agent's general toxicity, as well as toxicity related to damage to the kidneys and nerves (nephrotoxicity and neurotoxicity, respectively). Information on whether a chemical produces reactive free radicals could also give some clues about that agent's potential ototoxicity. Glutathione is an important cellular antioxidant that limits cell damage by reactive oxygen species. An antioxidant is a molecule capable of slowing or preventing the oxidation of other molecules (free radicals or reactive oxygen species—ROS). Antioxidants can be used to help treat or prevent some medical conditions, such as coronary artery disease, some cancers, macular degeneration, Alzheimer's disease, and some arthritis-related conditions. Antioxidants include some vitamins (such as vitamins C and E), some minerals (such as selenium), and flavonoids, which are found in plants. The best sources of antioxidants are fruits and vegetables.

Evidence is available indicating that ototoxicity due to noise plus carbon monoxide or hydrogen cyanide exposure (a combustion by-product) also involves free radicals. For this reason, information on certain chemicals being associated with free radicals or glutathione depletion could also help in the decision to examine a chemical for potential ototoxicity.

Until now few human studies have examined the time necessary for chemical exposures to affect the auditory system, and there is still uncertainty regarding whether it is a chronic or acute process. It is possible that a single, extremely high exposure, as in the case of someone who sniffs glue, will cause hearing loss, as one of the consequences of the abuse. Such high exposures are unlikely to happen in the workplace. Investigations which examined the effects of solvents over time indicated that hearing loss is observable two to three years earlier than is usually seen with noise exposure. Five or more years of noise exposure seem necessary for some individuals to develop hearing loss following occupational exposures. The time needed for a chemical exposure to cause hearing loss is certainly dependent on the specific ototoxicant and the characteristics of the exposure, and needs further investigation.

Considering that environmental and occupational factors other than noise can affect hearing, one needs to rethink which steps can be taken to prevent any hearing disorders. Some of theses steps will be discussed next.

Strategies for Protecting your Hearing From the Effects of Ototoxic Chemicals

The initial steps of hearing loss prevention programs are hazard assessment and control. It is important to learn if and what hazardous exposures exist in a workplace. Whenever hazardous noise or chemicals exist in the workplace, measures to reduce exposure levels to protect exposed workers and to monitor the effectiveness of these intervention processes are required by law. Some of these requirements are presented in Chapters 1 and 9 and you should become familiar with them. The most effective way to prevent hearing disorders from noise or chemical exposure is to remove the source of hazardous exposures from the workplace, for example, by engineering controls, use of personal protective equipment, or finding alternatives to minimize exposure, (such as reducing the duration of exposure). If the use of personal protective equipment is required, they should be worn as directed. Information on what equipment is adequate for obtaining needed protection can be found at the following two NIOSH URLs:
http://www.cdc.gov/niosh/topics/chemical.html
http://www.cdc.gov/niosh/topics/noise/abouthlp/chooseprotection.htm

Noise regulations pertaining to individuals in the US vary depending on the agency or branch of government having jurisdiction. Among the important ones to know is the level of noise exposure that is permissible. The OSHA Standard for Manufacturing requires that in environments where noise exposure reaches or exceeds 85 dB A workers must be placed in a hearing conservation program. As part of these programs, annual hearing tests are required (http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=standards&p_id=9735)

These and other preventive strategies that are used to protect workers from noise exposure will not necessarily protect workers from the effects of chemical exposures. When evidence that chemicals in the workplace can affect hearing is considered, then hearing loss prevention initiatives may be needed even in workplaces where noise exposure does not exceed 85 dB A.

Since 1998, the American Conference of Governmental Industrial Hygienists[1] in its publication includes a note in its Noise Section which states, “In settings where exposure to toluene, lead, manganese or n-butyl alcohol occurs, periodic audiograms are advised and should be carefully reviewed.” It also lists other aims to develop

specific recommendations and disseminate information addressing hearing loss prevention strategies that are not limited to exposures to excessive noise levels. A similar recommendation can be found in an Australian and New Zealand publication[2] requiring hearing tests for those exposed to ototoxic agents.

Also since 1998, the US Army has added ototoxic chemical exposure to their risk criteria in their hearing conservation program, particularly when in combination with even marginal noise. More recently, the US Army recommends audiometric monitoring for workers whose airborne exposures are at 50% of the most stringent criteria for occupational exposure limits to toluene, xylene, styrene, n-hexane, organic tin, carbon disulfide, mercury, organic lead, hydrogen cyanide, diesel fuel, kerosene fuel, jet fuel, JP-8 fuel, organophosphate pesticides, or chemical warfare nerve agents, regardless of the noise level. The 50% cut-off, while somewhat arbitrary, seems reasonable and may be a good place to start. When dermal exposures to these agents result in a systemic dose equivalent to 50% or more of the occupational exposure limit, yearly audiograms were also recommended. If a worker is currently participating in a hearing conservation program due to excessive noise, the reviewers of the audiometric data were recommended to be alert to possible additive, potentiating, or synergistic effects between the exposure to noise and the chemical substance, and if necessary, suggest reducing the exposure to one or both (http://chppm-www.apgea.army.mil/documents/FACT/51-002-0903.pdf).

Regardless whether hearing tests are offered at work or not, if you suspect a hearing loss, you should see an audiologist. It's important to give information to your audiologist on all exposures that can represent a risk to your hearing.

References

1. *Threshold Limited Values and Biological Exposure Indices* (TLVs® and BEIs®). (1998-1999) American Conference of Governmental Industrial Hygienists (ACGIH), Cincinnati, p. 114.

2. *Australia-New Zealand AS/NZS 1269:2005 Occupational Noise Management/Informative Appendix on Ototoxic Agents.* Standards New Zealand, Wellington: NZ, p. 25.

Suggested Readings

Phaneuf R, Hetu, R. (1990) An epidemiological perspective of the causes of hearing loss among industrial workers. *Journal of Otolaryngology* 19 (1): 31-40.
Morata TC, Franks JR, Dunn DE. (1994) Unmet needs in occupational hearing conservation. *The Lancet* 344 (8920): 479.
Fuente A and McPherson B. (2006) Organic solvents and hearing loss: The challenge for audiology. *International Journal of Audiology* 45 (11):367-81.
Morata TC. (2007) Promoting hearing health and the combined risk of noise-induced hearing loss and ototoxicity. *Audiological Medicine* 5 (1): 33–40.

http://chppm-www.apgea.army.mil/documents/FACT/51-002-0903.pdf
This website contains a fact sheet regarding ototoxic chemical exposures and guidelines for hearing conservation developed by the U.S. Army.

Acknowledgements

This chapter is dedicated to the memory of Dr. Derek E. Dunn

Disclaimer: The findings and conclusions in this chapter are those of the author and do not necessarily represent the views of the National Institute for Occupational Safety and Health.